IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:

Barkur G. Bhat *et al.*

Appln. No.: 09/267,199

Filed: March 12, 1999

For: **Nucleic Acid Molecules and Other Molecules Associated with the Tocopherol Pathway**

Art Unit: 1631

Examiner: Marjorie A. Moran

Atty. Docket: 16517.233

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APPELLANT'S BRIEF

Commissioner for Patents
Washington, DC 20231

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-described patent application. A Notice of Appeal was filed on July 10, 2002. Authorization to charge the official fees for this filing, including extension of time fees, is given in the accompanying transmittal letter. *This Brief is submitted in triplicate.*

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant is unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 10-18 and 20-25 are pending. Claims 1, 2 and 26 are cancelled without prejudice in the Amendment After Final Rejection filed herewith and discussed *infra*. Claims 10-12 and 16 are amended in the Amendment. Claims 10-18, 20-22 and 24-25 stand finally rejected under 35 U.S.C. §§ 101 and 112, first paragraph. Claim 23 stands finally rejected under 35 U.S.C. § 112, first paragraph. Claim 10 additionally stands finally rejected under 35 U.S.C. § 102. Applicants appeal all of the rejections of each of the claims.[1]

4. Status of Amendments

Applicants' representative conducted an interview with the Examiner on September 17, 2002, in which proposed amendments to the claims were discussed. *See* Interview Summary mailed September 17, 2002 (Paper Number 18). An Amendment After Final Rejection (the "Amendment") has been filed concurrently herewith canceling claims 1, 2 and 26 and amending claims 10-12 and 16. The Amendment is intended to clarify the issues with respect to the rejection of the claims under 35 U.S.C. §§ 102 and 112, first and second paragraphs.

5. Summary of Invention

The invention is directed to a nucleic acid molecule comprising a sequence that hybridizes under conditions of 2.0 X sodium chloride/sodium citrate (SSC) at about 65°C to a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOs: 100, 147, 153, 161, 180, 199, 232 and complements thereof. Specification at page 23, lines 4-8 and at page 60, line 16 through page 61, line 10. The invention is also directed to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199, 232. Specification at page 23, line 4 to page 26, line 17. The invention is also directed to a nucleic acid molecule consisting of a nucleic acid

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[1] Applicants additionally note that claim 2 stands finally rejected under 35 U.S.C. §§ 101 and 112, first paragraph; claim 1 stands finally rejected under §§ 102 and 112, first paragraph; and claim 26 stands finally rejected under 35 U.S.C. §§ 101 and 112, first and second paragraphs. As these claims have been cancelled without prejudice, *see* Amendment (filed herewith), Applicants do not address the merits of these rejections in this brief.

sequence selected from the group consisting of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199, 232. *Id.* The invention is also directed to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1. *Id.* The invention is also directed to a nucleic acid molecule that encodes a maize shikimate dehydrogenase or fragment thereof. Specification at page 25, lines 7-14. The invention is also directed to a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 158 or complement thereof. *Id.*

6. Issues

The issues in this Appeal are:

(a) whether claims 10-18, 20-22, and 24-25 are unpatentable under 35 U.S.C. § 101 for allegedly being unsupported by a specific asserted utility or a well established utility;

(b) whether claims 10-18, 20-22, and 24-25 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because the claimed invention purportedly lacks utility;

(c) whether claims 23-24 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged insufficiency of written description;

(d) whether claims 10-18 and 20-24 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged insufficiency of written description;

(e) whether claim 24 is unpatentable under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because undue experimentation would supposedly be required to make and/or use the claimed nucleic acid molecules; and

(f) whether claim 10 is unpatentable under 35 U.S.C. § 102(b) for alleged anticipation.

7. Grouping of Claims

Claims 10-18 and 20-25 remain in this case. Claims 10, 12, 16, 22, 23 and 25 are independent. All of the claims at issue do not stand or fall together. The separate patentability of the claims is addressed in Sections 8.A through 8.G below. A copy of the currently pending claims on appeal prior to the Amendment After Final Rejection is attached hereto as Appendix

A. A copy of the claims as amended in the Amendment After Final Rejection filed concurrently herewith is attached hereto as Appendix B.

8. Argument

A. Summary of Appellant's Position

As the Supreme Court said in *Brenner v. Manson*, the "basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility....where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Applicants have met their part of the bargain – they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example use to identify the presence or absence of a polymorphism in a population of maize or soybean plants. This benefit is specific, not vague or unknown, and it is a "real world" or substantial benefit. Because the claimed nucleic acid molecules provide at least these benefits, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed nucleic acid molecules for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Furthermore, Applicants' disclosure provides, for example, nucleic acid molecules that encode for a maize shikimate dehydrogenase or fragment thereof, as recited in claim 23. The specification asserts that at least one nucleic acid molecule of the present invention, *i.e.*, a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 158, encodes a maize shikimate dehydrogenase or fragment thereof. *See* Table A. Accordingly, because the specification demonstrates that Applicants had possession of (and have provided an adequate description of) the claimed nucleic acid molecules of claims 23 and 24, the written description requirement of 35 U.S.C. § 112, first paragraph, has been met.

Additionally, Applicants have provided an adequate description of the claimed nucleic acid molecules that demonstrates Applicants' possession of the claimed invention of claims 10-

18 and 20-24. The genera of claimed nucleic acid molecules, *e.g.*, the genus of nucleic acid molecules comprising the nucleic acid sequences of SEQ ID NOs: 100, 147, 153, 161, 180, 199 and 232 of claim 10, for example, have been described by the recitation of common structural features, *e.g.*, the nucleotide sequences of SEQ ID NO s: 100, 147, 153, 161, 180, 199 and 232, which distinguishes molecules in the claimed genera from molecules not in the claimed genera.[2] Because the specification demonstrates that Applicants had possession of (and have provided an adequate description of) the claimed genera of nucleic acid molecules, the specification satisfies the written description requirement of 35 U.S.C. § 112.

Applicants have asserted that the claimed nucleic acid molecules actually work for the utilities disclosed and described in the specification, and so the enablement rejection of claim 24 must be reversed. Applicants have asserted that one skilled in the art is able to use the claimed nucleic acid molecules for at least two disclosed utilities, namely use to identify the presence or absence of a polymorphism and use as a hybridization probe for expression profiling. *See, e.g.*, specification at page 84, line 18 through page 92, line 11, and at page 97, line 22 to page 98, line 18. Moreover, Applicants have asserted in the specification that, for example, a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 158 would encode a maize shikimate dehydrogenase or fragment thereof. *See* Table A. The law clearly establishes that the enablement requirement is satisfied if at least one mode of making and using the invention is enabled. Because Applicants have asserted that the claimed nucleic acid molecules work for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Finally, Claim 10 was erroneously rejected as anticipated by two references which fail to teach any of the recited nucleic acid sequences. The Examiner improperly considered non-identical chemical compounds to anticipate the claim, despite the fact that the references fail to teach the chemical composition of SEQ ID NO: 1 or its complement. Moreover, the rejection is

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[2] This assertion applies with equal force to all of the nucleic acid molecules of the present invention, including, for example, nucleic acid molecules comprising the nucleic acid sequences of SEQ ID NOs: 158 and 184 as in claim 22, and nucleic acid molecules comprising the nucleic acid sequence of SEQ ID NO: 1 as in claim 12.

not based on what exists in the art or what the art teaches, but rather on the Examiner's theory, unsupported by any evidence, that the art sequence *might* anticipate the claims. Such clearly unsupported conjecture is simply not a proper basis for an anticipation rejection.

B. The Claimed Nucleic Acids Have Legal Utility

Pending claims 10-18, 20-22, and 24-25 were erroneously rejected under 35 U.S.C. § 101 as allegedly not supported by either a "specific, substantial and credible utility or by a well established utility." Final Action mailed April 10, 2002 (Paper No. 16) ("Final Action") at page 3. Furthermore, although the Final Action admits that the specification clearly asserts "that the claimed nucleic acid molecules encode tocopherol synthesis pathway enzymes or fragments thereof", among the other various utilities asserted in the specification, these uses supposedly fail to meet the utility requirement because "it is unknown whether any sequence is actually translated into a peptide, or, if translated, what the activity or function of that peptide may be." *Id.* at page 4. According to the Final Action, in order for the claimed nucleic acid molecules to have utility, "the identity and activity of the peptide must be known or established." *Id.*

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide <u>one</u> identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

The courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip*, 185 F.3d at 1366, 51 USPQ.2d at 1702. For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the

invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Applicants have asserted in the specification that the claimed nucleic acid molecules provide identifiable benefits, for example, use to identify the presence or absence of a polymorphism, and use as a hybridization probe for expression profiling. *See, e.g.*, specification at page 84 line 18 through page 92, line 11, and page 97, line 22 to page 98, line 18. Either of these utilities described alone is enough to satisfy Section 101. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Nucleic Acid Molecules Provide A Specific Benefit, *i.e.*, They Have Specific Utility

The Examiner acknowledges that the specification describes multiple utilities for the present invention, including "probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to make the corresponding antibodies, gene mapping, isolation of homologous sequences, detection of gene expression such as in Northern blot analysis, molecular weight markers, chromosomal markers, and for numerous other generic genetic engineering usages." Office Action mailed November 21, 2000 (Paper Number 7), at page 5. Furthermore, the Examiner acknowledges that it is well known in the art that polynucleotides "can be used in hybridization assays to obtain other (e.g. homologous or complementary) nucleic acid sequences, to identify polymorphisms, etc." Office Action mailed October 17, 2001 (Paper Number 14), at page 1. Moreover, the specification also discloses

additional utilities for the claimed nucleic acid molecules,[3] including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for phenotypic variations in tocopherol levels and synthesis in a variety of plants. Specification at page 11, lines 12-23 and at page 128, line 6 through page 131, line 9. For example, a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored. Such a screen is analogous to a cell-based assay, which has a legally sufficient utility.[4] Other utilities disclosed in the specification include use of the claimed nucleic acid molecules to measure the level of mRNA in a sample,[5] and use as molecular markers.[6]

(a) Identifying the Presence or Absence of a Polymorphism

More particularly, one of the utilities disclosed in the specification is use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism. Specification at page 84, line 18 through page 92, line 11. The Examiner argues that this utility, like many of the asserted utilities, is not specific or substantial, *see e.g.,* Office Action mailed October 17, 2001, at

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[3] It is irrelevant whether the corresponding mRNA or polypeptide have utility because Applicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules.

[4] *See, e.g.*, MPEP § 2107 at page 2100-32.

[5] It is standard practice to screen populations of nucleic acids with EST sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, tocopherol production and quality in a plant. Contrary to the Examiner's assertions, this use is not using the claimed nucleic acid molecules to identify a " 'real world' context or use." *See* Office Action mailed November 21, 2000, at page 6. It is a **use** of the claimed nucleic acid molecules in a real world context.

[6] One can use the claimed nucleic acid molecules to determine location of a corresponding DNA sequence on a physical map or genetic map location without knowing anything beyond the claimed sequence. The use of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits.

page 1, but does not provide any support (legal or factual) for the proposition that detection of polymorphisms using the claimed nucleic acid molecules is not a legal utility.

Many of the disclosed utilities in this case, including the detection of polymorphisms, are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The Examiner denigrates such utilities by asserting that these utilities are not "useful" because "the question of utility is not based on inoperability of a portion of a nucleic acid, but rests on whether the claimed nucleic acids, themselves, have utility, or encode proteins which have utility." Final Action at page 5. However, the fact that, *e.g.*, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107 at page 2100-33.

Use of the claimed nucleic acid molecules to detect the presence or absence of polymorphisms is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[7] Likewise, the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usefully demonstrates that the two (or more) populations being compared share a common genetic heritage.

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[7] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

Moreover, the use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism has particular relevance to the manipulation and expression of enzymes in the tocopherol pathway and in the production of tocopherol content in a plant. Applicants have disclosed that nucleic acid molecules of the present invention comprise sequences that encode enzymes of the tocopherol pathway or fragments thereof. *See*, for example, specification at page 62, lines 13-16 and Table A. The specification also discloses that the instant nucleic acids can be used for cosuppression (*e.g.*, page 50, lines 5-13) or antisense suppression (*e.g.*, page 130, line 4 to page 131, line 9), and are useful in altering the levels of enzymes of the tocopherol synthesis pathway. As such, the use of the claimed nucleic acid molecules in the isolation of chromosomes or determining the genotype of an individual plant strain clearly has an identifiable benefit. Applicants submit that the use of the claimed sequences in this manner is analogous to the use of labeled monoclonal antibodies for the isolation of cells in flow sorting in the first instance, and phenotypic/genotypic analysis in the second instance (*see, for example,* Leitch *et al., Nuc. Acid Res.* 20(8):1897-901 (1992)) (Exhibit A). Both flow sorting and genotypic analysis ultimately have "real world" value at least on the breeding and selection of plants, although other utilities can be envisioned.

The claimed nucleic acid molecules have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, to identify the presence or absence of a polymorphism. This benefit is immediately realized directly from the use of the claimed nucleic acids, not from the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Probes for Other Molecules or Source for Primers

Other uses for the claimed nucleic acid molecules are as probes for other molecules or as a source of primers. Although the Examiner admits that "a unique nucleic acid sequence may be used to identify a unique subset of related sequences", the Examiner suggests that these uses are not legal utilities because "as the utility for the 'original' nucleic acid sequence is unknown, the

unique subset itself has no known utility." Office Action mailed October 17, 2001, at page 2. This is not correct. The specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms such as alfalfa, *Arabidopsis*, barley, *Brassica*, cotton, sunflower, *Phaseolus*, etc.[8] Specification at page 82, lines 3-18. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and thus has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

Furthermore, Applicants assert that nucleic acid molecules of the present invention comprise sequences that encode enzymes of the tocopherol pathway or fragments thereof. *See*, for example, specification at page 62, lines 13-16 and Table A. Modulation of tocopherol content (including vitamin E) of plant tissues and changes in the levels of the enzymes in the tocopherol pathway can alter both the tocopherol content as well as the compositional quality of the vitamin E family members produced (*see, e.g.,* specification at page 2, lines 4-8). Thus, the use of the claimed nucleic acid molecules as probes or a source of primers have particular relevance to the identification of nucleic acid molecules comprising nucleic acid sequences encoding enzymes in this pathway.

Another illustrative example of a molecule that can be isolated using a claimed nucleic acid molecule is the promoter of the gene corresponding to that claimed nucleic acid molecule. Applicants have specifically disclosed that one use of the claimed nucleic acid molecules is to initiate a chromosome walk. Specification at page 83, line 14 through page 84, line 3. The Examiner denigrates that utility by asserting that the "specification teaches only general uses

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[8] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Applicants to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules.

(purposes), but does not teach any specific 'purpose' for the claimed SEQ ID NO's." Office Action mailed October 17, 2001, at page 1.

In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose, *i.e.,* chromosome walks. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not "specific" to the claimed nucleic acid molecules. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter in, for example, maize or soybean that is associated with the tocopherol synthesis pathway. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a <u>better</u> starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules. An invention may be "less effective than existing devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed nucleic acid molecules could not be so used. Accordingly, the assertion of this

utility as a probe for other molecules or as a source of primers satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(2) The Claimed Nucleic Acid Molecules Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also appears to assert that the disclosed uses are legally insufficient because they are not "substantial" utilities. Final Action at pages 3-4. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). " 'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[9]

There can be no question that one skilled in the art can use the claimed nucleic acid molecules in a manner which provides an immediate benefit to the public, for example to detect the presence or absence of polymorphisms. The detection of polymorphisms provides an immediate benefit to the public because, *e.g.*, it enables a plant breeder to determine the distribution of parental genetic material in the progeny of a cross. This information about a plant's genetic profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

Quite apart from the detection of polymorphisms, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to such nucleic acid molecules. The utility of ESTs is not merely an academic issue; the real world value of ESTs is self-evident from the growth of a multi-million dollar

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[9] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

industry in the United States premised on the usefulness of ESTs. Like fermentation processes involving bacteria, ESTs and nucleic acid molecules with EST sequences are "industrial product[s] used in an industrial process – a useful or technical art if there ever was one." *In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for EST products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Cf. Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) ("People rarely, if ever, appropriate useless inventions"). Quite simply, the commercial value of ESTs is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

(3) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.[10] A challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of

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[10] Examples of incredible utilities are given in MPEP § 2107 at page 2100-34, and include:

> an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107 at 2100-40.

Applicants have explicitly identified specific and substantial utilities, not only in the specification, but in Applicants' Response dated March 19, 2001, at pages 6-7 and in Applicants' Response dated January 17, 2002, at pages 6-7. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed nucleic acid molecules will not work for the disclosed utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of claims 10-18, 20-22 and 24-25 under 35 U.S.C. §101 is improper and should be reversed.

C. The Claimed Nucleic Acids Are Enabled by the Specification

The enablement of the claimed nucleic acid molecules has been challenged. Claims 10-18, 20-22 and 24-25 were erroneously rejected as not enabled by the specification, because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled. Final Action at page 5. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut

the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

D. The Specification Provides an Adequate Written Description of the Claimed Nucleic Acid Molecules of Claims 23 and 24

The Examiner has erroneously imposed a rejection of claims 23 and 24 under 35 U.S.C. § 112, first paragraph, because they allegedly are directed to subject matter "which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Final Action at page 6. While the Examiner admits that "the nucleic acid sequences represented by the claimed SEQ ID NO's are fully described by the specification at the time of filing, nucleic acid sequences *encoding the proteins* recited in claims 1 and 23 were not fully described". Final Action at page 7 (emphasis in original).

This assertion is not correct. It is well-settled law that an adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000); MPEP § 2163 at 2100-160. The function of the written description requirement is to ensure that the inventor had possession of the specific subject matter claimed; how the specification accomplishes this is not material. *In re Herschler*, 591 F.2d 693, 700-01, 200 USPQ 711, 717 (C.C.P.A. 1979); *In re Kaslow*, 707 F.2d 1366, 707 F.2d 1366, 217 USPQ 1089 (Fed. Cir. 1983); MPEP § 2163 - § 2163.04.

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498,

1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if every nuance of the invention was not expressly described, then the written description requirement has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. After reading the present specification, a person of ordinary skill in the art, *e.g.*, a molecular biologist, would understand that Applicants had possession of a nucleic acid molecule that encodes a maize shikimate dehydrogenase or fragment thereof.

Claim 23 is directed to a substantially purified nucleic acid molecule that encodes a maize shikimate dehydrogenase or fragment thereof. The specification provides the nucleic acid sequence of SEQ ID NO: 158, as well as how to construct cDNA libraries using the claimed nucleic acid molecules (*see, e.g.,* specification at page 12, line 7 through page 14, line 10 and Examples 1-3); and provides a functional characterization of each disclosed sequence based on the enzyme encoded by each sequence (*see, e.g.,* specification at page 66, line 8 through page 68 line 22 and Table A). Additionally, the specification sets forth the functional characterization based on the homology of the claimed sequences to known coding sequences for enzymes in the tocopherol pathway (*see, e.g.,* specification at page 168, line 13 through page 171, line 10 and Example 4). Furthermore, nucleic acids encoding tocopherol synthesis pathway enzymes, or fragments thereof, are addressed at length in the disclosure at page 22, line 14 through page 34, line 21, and at page 58, line 12 through page 76, line 22.

The Final Action asserts that "homology alone is not is not evidence that a particular protein is encoded by a recited nucleic acid sequence". To support this position, the Examiner relies on IBBA (TIBS (2002)), vol. 27(2), page 64. This article is directed to the controversy in the art in *general* over prediction of function based on homology alone, but does not take into consideration Applicants' disclosure. The Examiner has not presented any evidence to properly

address Applicants' specific arguments with respect to the present disclosure. *See* MPEP § 2163.04 at page 2100-169.

The present specification discloses that SEQ ID NO: 158 exhibits 69% sequence identity with a nucleic acid sequence known to encode a maize shikimate dehydrogenase. *See* Table A at page 240. The Examiner has offered no evidence to demonstrate why one of ordinary skill in the art would reasonably doubt that a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 158 would encode a maize shikimate dehydrogenase or fragment thereof and, as such, has not met the burden to impose a written description rejection. *See, e.g., In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (C.C.P.A. 1976), *In re Marzocchi*, 439 F.2d 220,224, 169 USPQ 367, 370 (C.C.P.A. 1971), *In re Alton*, 76 F.3d 1168, 1176, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996). Therefore, the rejection of claims 23 and 24 under 35 U.S.C. §112, first paragraph, is improper and should be reversed.

E. The Specification Provides an Adequate Written Description of the Claimed Invention

Despite the Examiner's admission that the specification describes SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 199 and 232 (Final Action at page 7)[11], the adequacy of the written description has been challenged by the Examiner with respect to claims 10-18 and 20-24 as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Final Action at page 7. The basis for the Examiner's challenge is that the claims "recite open claim language (i.e. comprising, comprises, or having) and are therefore also directed to encompass gene sequences, sequences that hybridize SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232, corresponding sequences from other species, derivatives, allelic variants, splice variants, and so forth...The specification provides insufficient written description to support the genus

[11] Applicants have also disclosed the nucleic acid sequence of SEQ ID NO: 184 in the present specification.

encompassed by the claims." *Id.* This is not a proper basis for a written description rejection of a "comprising" claim. If it was, every "comprising" claim ever written would be invalid for failing to describe every nuance of the claimed invention. Furthermore, the specification demonstrates to one skilled in the art that Applicants were in possession of the claimed genera of nucleic acid molecules.

(1) The Specification Reflects Applicants' Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if every nuance of the invention was not expressly described, then the written description requirement has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. After reading the present specification, a person of ordinary skill in the art, *e.g.*, a molecular biologist, would understand that Applicants had possession of nucleic acid molecules comprising SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232.

Applicants have provided the nucleic acid sequences required by the claims, *i.e.*, SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232, as well as, for example, vectors comprising the nucleic acid sequence (*see, e.g.,* specification at page 111, line 6 through page 119, line 12, and at page 132, line 16 through page 138, line 4), hybridization conditions which may be used with the nucleic acid molecules of the present invention (*see, e.g.,* specification at page 60, line 16 through page 61, line 10), and binary artificial chromosomes (BIBACs) and other systems that may be used to introduce the claimed nucleic acid molecules into a host cell (*see, e.g.,* specification at page 119, lines 13-20). The fact that the claims at issue are intended to

cover molecules that include the recited sequence joined with additional sequences, or that hybridize under specific conditions to the recited sequence does not mean that Applicants were any less in possession of the claimed nucleic acid molecules.[12] It is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

The present application describes more than just the nucleotide sequences required by the claims (SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232). For example, it describes vectors comprising the claimed nucleic acid molecules (specification at page 111, line 6 through page 119, line 12, and at page 132, line 16 through page 138, line 4), and describes how to make the nucleotide sequences and the libraries from which they were originally purified. *See, e.g.,* specification at page 12, line 7 through page 14, line 10 and Examples 1-3. Furthermore, the addition of extra nucleotides or detectable labels to the disclosed nucleotide sequences (SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232) is readily envisioned by one of ordinary skill in the art upon reading the present specification,[13] in particular at page 76, line 21 through page 77, line 8 (describing fusion peptide molecules encoded by the claimed nucleic acid molecules), page 69, line 20 through page 72, line 2 (describing the identification of single nucleotide polymorphisms (SNPs)), page 105, line 15 through page 107, line 7 (describing site directed mutagenesis) and page 163, line 22 through

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[12] If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then she goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

[13] It is established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *E.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

page 164, line 6 (citing references describing the construction, manipulation and isolation of nucleic acid macromolecules). Moreover, it is well established that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981)).

(2) Applicants Have Described the Claimed Invention

The Final Action asserts that because Applicants have not disclosed any "sequences/structures, such as corresponding sequences from other species derivatives, allelic variants, splice variants, and so forth", Applicants have allegedly not adequately disclosed the claimed genus. Final Action at page 8. The Examiner appears to assert that each nucleic acid molecule within the claimed genus must be described by its complete structure. These assertions are totally unfounded. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Applicants have satisfied that test for written description.

In particular, Applicants have disclosed common structural features, for example, the nucleotide sequences of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232. The respective common structural feature (the nucleotide sequences of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232) is shared by <u>every</u> nucleic acid molecule in the claimed genera, and it distinguishes the members of the claimed genera from non-members. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 1, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1.[14] If a nucleic acid molecule does not contain SEQ ID

[14] The same argument applies with equal force to every genus of the claimed nucleic acid molecules. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 100, then it is a

NO: 1, then it is not a member of that claimed genus. The presence of other nucleotides at either end of the recited sequence will not interfere with the recognition of a claimed nucleic acid molecule as such – it either contains the nucleotides of SEQ ID NO: 1 or it does not. One skilled in the art, after reading the present specification, would clearly know if a nucleic acid molecule contains one of the recited nucleotide sequences. Thus, claims 10-18 and 20-24 are supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, and the rejection should be reversed.

F. The Claimed Invention Is Enabled by the Specification

Claim 24 was rejected in the Final Office Action under 35 U.S.C. §112, first paragraph, because the subject matter allegedly was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Applicants respectfully disagree.

The Examiner has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original).

The Final Action asserts that claim 24 is not enabled because "homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence". Final Action at page 9. However, the only support cited in the Final Action to substantiate this assertion is directed to the *general* controversy in the art to predict function based on homology. *See* Section 8.D, *supra*. Applicants reiterate the present specification discloses that SEQ ID NO: 158 exhibits 69% sequence identity with a nucleic acid sequence known to encode a maize shikimate dehydrogenase. *See* Table A at page 240. The Examiner has offered no evidence to

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member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 100. *See, e.g.*, claim 13.

demonstrate why one of ordinary skill in the art would reasonably doubt that a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 158 would encode a maize shikimate dehydrogenase or fragment thereof and, as such, has not met the burden to impose an enablement rejection. To the contrary, Applicants submit that an analysis of the criteria presented by *In re Wands* supports Applicants' position that no undue experimentation would be required to make and use the claimed invention. *See In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1998).

The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, identification of an active site, and radiometric synthase assay conditions, to which a person of ordinary skill in the art has access. The Final Action asserts that undue experimentation would be required because "[t]he instant specification does not disclose any amino acid sequences" and, thus, it would allegedly require "undue experimentation for one skilled in the art to determine how to generate the peptides, with the functionality claimed, from the disclosed nucleic acid sequences." Final Action at page 9. However, one skilled in the art is sufficiently guided by Applicants' disclosure, which sets forth the data base and parameters employed to generate the homology data in Table A (*see, e.g.,* Example 4).

The Final Action further asserts that "while assays to determine kinase activity are known in the art, each is specific to a particular substrate...therefore one skilled in the art would have to develop an assay to determine if a kinase with the claimed functionality and specificity...were indeed produced." Final Action at page 9. As stated above, practitioners in the art are guided by the high level of skill in the art and the present disclosure of the specification (*see, e.g.,* specification at page 128, lines 6-16). Performing routine and well-known steps, such as sequence alignment protocols, molecular weight determination, and antibody hybridization assays, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 218-219 (C.C.P.A. 1976).

The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. Again, the specification provides evidence of sequence identity, discloses start and stop positions within a sequence, and discusses the use of the claimed SEQ ID NO to isolate additional sequences within a genome. *See, e.g.,* Examples 1-4 and Table A. Based on such disclosure, one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with claim 24.

The fourth, fifth, and sixth *Wands* criteria focuses on the nature of the invention, the state of the art, and the relative skill in the art. The Final Action acknowledges the level of skill in the art is high. Final Action at page 9. Furthermore, claim 24 relates to a nucleic acid molecule encoding a maize shikimate dehydrogenase or fragment thereof comprising the nucleic acid sequence of SEQ ID NO: 158. The specification provides a detailed description of the nucleic acid sequence required by the claim, and further describes amino acid sequences derived therefrom, and constructs and methods of use related thereto. *See, e.g.*, specification at page 73, line 15 through page 77, line 22 (describing polypeptide molecules encoded by the nucleic acid sequences of the present invention, homologues and other modifications, and methods of producing or expressing peptides or fragments of peptides), and page 111, line 6 through page 120, line 11 (describing use of the claimed nucleic acid molecules in methods of transforming plants). Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to identify, confirm, and introduce into other hosts, nucleic acid and amino acid sequences.

The seventh criterion considers the predictability of the art. The Final Action argues that the "one skilled in the art must 'guess' at some information (e.g., open reading frames, actual start codon, homology parameters) and/or develop new assays to arrive at the claimed invention". Final Action at page 10. Applicants respectfully disagree and assert, as discussed *supra*, that the specification discloses sufficient guidance to render the results of substitutions, additions, and deletions within the claimed SEQ ID NO predictable. *See, e.g.,* specification at

page 64, line 12 through page 66, line 7. Furthermore, the specification provides sufficient guidance to one of skill in the art to decipher the information necessary to make and use the claimed nucleic acid molecules. *See, e.g.,* specification at page 168, line 13 through page 171, line 10 (describing software that can be used to identify open reading frames within the claimed nucleic acid molecules), and page 128, line 6-17 (citing references to develop assays for gene expression).

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). In the present case, one of skill in the art is specifically guided by the disclosure to look to, *e.g.*, sequence identity data in making that determination.

The Examiner has provided neither evidence supporting the rejection nor any explanation of why the specification allegedly fails to enable the nucleic acid molecules of claim 24. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement). Therefore, because the above analysis illustrates that the specification clearly enables at least the methods of making and using the invention as set forth in the Examples, the enablement requirement has been satisfied. *Cf. Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) ("the enablement requirement is met if the description enables <u>any</u> mode of making and using the invention") (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Accordingly, the enablement rejection under 35 U.S.C. § 112, first paragraph, is improper and must be reversed.

G. The Claimed DNA Constructs are Novel

Claim 10 was erroneously rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by BAYSDORFER (Genbank accession No. AA661448, November 12, 1997) in the Final Action. According to the Final Action, "BAYSDORFER teaches an mRNA sequence from maize encoding 3-deoxy-d-arabino-heptulosonate 7-phosphate synthase". Final Action at page 10. The Examiner asserts that the references discloses "an mRNA with complementarity to the instant SEQ ID NO: 1, and would be expected to hybridize to SEQ ID NO: 1 under the conditions recited in the instant claim 10". *Id.* Applicants disagree with the rejection.

This reference does not anticipate the present claims. For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 677, 7 U.S.P.Q. 2d 1315, 1317 (Fed. Cir. 1988). *See also Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). BAYSDORFER does not teach every element of the claimed invention.

The Examiner contends that BAYSDORFER would be expected to hybridize to SEQ ID NO: 1 under the conditions recited in claim 10, but presents no evidence to support this position. Instead of providing evidence, the Examiner appears to shift the burden of proof to Applicants to provide evidence that BAYSDORFER would not hybridize to SEQ ID NO: 1 under the claimed hybridization conditions. This is not the law. Furthermore, the Examiner has also asserted that the cited reference has some homology to SEQ ID NO: 1, but has not disclosed the extent of the homology. This assertion is insufficient to establish an assertion that the cited reference anticipates claim 10.

Because the chemical disclosed in the BAYSDORFER reference is not the same as the chemical disclosed as SEQ ID NO: 1, every element of the claimed invention has not been identically shown in the reference. *See Diversitech Corp.*, 850 F.2d at 677, 7 U.S.P.Q.2d at 1317. Accordingly, the BAYSDORFER reference does not anticipate claim 10.

Although Applicants strenuously disagree with the rejection of claim 10 under 35 U.S.C. § 102(b), to facilitate prosecution, claim 10 has been amended. As such, the rejection of claim 10 under 35 U.S.C. § 102(b) over BAYSDORFER has been rendered moot.

Claim 10 was also erroneously rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by SASAKI (Genbank accession No. D39938, November 11, 1994) in the Final Action. According to the Final Action, "SASAKI teaches a cDNA sequence which is 87.7% identical to instant SEQ ID NO: 1, and would be expected to hybridize under the conditions recited in instant claim 10 to a complement of SEQ ID NO: 1". Final Action at page 10. Applicants disagree with the rejection.

This reference does not anticipate the present claims. For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *Diversitech Corp. v. Century Steps, Inc.,* 850 F.2d 675, 677, 7 U.S.P.Q. 2d 1315, 1317 (Fed. Cir. 1988). *See also Kalman v. Kimberly Clark Corp.,* 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied,* 465 U.S. 1026 (1984). SASAK does not teach every element of the claimed invention.

The Examiner contends that SASAKI would be expected to hybridize to SEQ ID NO: 1 under the conditions recited in claim 10, but presents no evidence to support this position. Instead of providing evidence, the Examiner appears to shift the burden of proof to Applicants to provide evidence that SASAKI would not hybridize to SEQ ID NO: 1 under the claimed hybridization conditions. This is not the law.

Because the chemical disclosed in the SASAKI reference is not the same as the chemical disclosed as SEQ ID NO: 1, every element of the claimed invention has not been identically shown in the reference. *See Diversitech Corp.*, 850 F.2d at 677, 7 U.S.P.Q.2d at 1317. Accordingly, the SASAKI reference does not anticipate claim 10.

Although Applicants strenuously disagree with the rejection of claim 10 under 35 U.S.C. § 102(b), to facilitate prosecution, claim 10 has been amended. As such, the rejection of claim 10 under 35 U.S.C. § 102(b) over SASAKI has been rendered moot.

Conclusion

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,

Date: October 10, 2002

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APPENDIX A

Pending Claims Prior to the Amendment After Final Rejection

1. A substantially purified nucleic acid molecule that encodes a maize or soybean tocopherol synthesis pathway enzyme or fragment thereof, wherein said maize or soybean tocopherol synthesis pathway enzyme is selected from the group consisting of:

(a) deoxyarabiono-heptulosonate-P-synthase or fragment thereof;

(b) putative deoxyarabiono-heptulosonate-P-synthase or fragment thereof;

(c) dehydroquinate synthase or fragment thereof;

(d) dehydroquinate dehydratase or fragment thereof;

(e) putative dehydroquinate dehydratase or fragment thereof;

(f) shikimate kinase or fragment thereof;

(g) chorismate synthase or fragment thereof;

(h) chorismate mutase or fragment thereof;

(i) tyrosine transaminase or fragment thereof;

(j) putative tyrosine transaminase or fragment thereof;

(k) transaminase A or fragment thereof;

(l) putative transaminase A or fragment thereof;

(m) homogentisic acid dioxygenase or fragment thereof; and

(n) geranylgeranylpyrophosphate synthase or fragment thereof.

2. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 199, and SEQ ID NO: 232.

10. An isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 2.0 X sodium chloride/sodium citrate (SSC) at about 65°C to a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOs: 1, 100, 147, 153, 161, 180, 199, and 232 and complements thereof.

11. The isolated nucleic acid molecule, according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 199, and SEQ ID NO: 232.

12. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1.

13. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 100.

14. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 147.

15. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 153.

16. An isolated nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 158 or complements thereof.

17. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 161.

18. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 180.

20. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 199.

21. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 232.

22. An isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 158, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 184, SEQ ID NO: 199, and SEQ ID NO: 232.

23. A substantially purified nucleic acid molecule that encodes a maize shikimate dehydrogenase or fragment thereof.

24. The substantially purified nucleic acid molecule according to claim 23, wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO: 158.

25. An isolated nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 158, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 184, SEQ ID NO: 199, and SEQ ID NO: 232.

26. An isolated nucleic acid molecule consisting essentially of residues selected from the group consisting of: residues 1-252 of SEQ ID NO: 1, residues 1-261 of SEQ ID NO: 100, residues 1-224 of SEQ ID NO: 147, residues 1-167 of SEQ ID NO: 153, residues 1-182 of SEQ ID NO: 158, residues 1-225 of SEQ ID NO: 161, residues 1-281 of SEQ ID NO: 180, residues 1-331 of SEQ ID NO:199, residues 1-245 of SEQ ID NO: 232 and complements of each.

APPENDIX B

Pending Claims as Amended in the Amendment After Final Rejection

10. An isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 2.0 X sodium chloride/sodium citrate (SSC) at about 65°C to a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOs: 100, 147, 153, 161, 180, 199, 232 and complements thereof.

11. The isolated nucleic acid molecule, according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 199, and SEQ ID NO: 232.

12. An isolated nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1.

13. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 100.

14. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 147.

15. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 153.

16. An isolated nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 158 or complement thereof.

17. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 161.

18. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 180.

20. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 199.

21. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 232.

22. An isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 158, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 184, SEQ ID NO: 199, and SEQ ID NO: 232.

23. A substantially purified nucleic acid molecule that encodes a maize shikimate dehydrogenase or fragment thereof.

24. The substantially purified nucleic acid molecule according to claim 23, wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO: 158.

25. An isolated nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 158, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 184, SEQ ID NO: 199, and SEQ ID NO: 232.